

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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(day/month/year) see form PCT/ISA/210 (second sheet)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION See paragraph 2 below

International application No.
PCT/GB2005/000560

International filing date (day/month/year)
17.02.2005

Priority date (day/month/year)
20.02.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/5377, A61K31/4439, A61K31/497, A61K31/4545, A61K31/4535, A61K31/4025, A61K31/40, A61K31/454,

Applicant
ASTRAZENECA AB

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
- claims Nos. 1,17,18

because:

- the said international application, or the said claims Nos. 1,17,18 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the whole application or for said claims Nos.
- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- has not been furnished
- does not comply with the standard

the computer readable form

- has not been furnished
- does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000560

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	14
	No: Claims	1-13,15-18
Industrial applicability (IA)	Yes: Claims	2-26
	No: Claims	1,17,18

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Cited Documents

D1: WO 98/02430
D2: WO 96/03383
D3: WO 00/53185

Section III

1. Claims 1, 17 and 18 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(I) PCT).

Section V

2. Having regard to the cited prior art, the subject-matter of claims 1-18 is novel.
3. The subject-matter of claims 1-13 and 15-18 does not meet the requirements of Art. 33(3) EPC.
- 3.1 The application contains only 12 preparative examples of compounds falling within the scope of the claims, and not a single example of biological (or other) activity.

Of these examples, in every case

R^1 is hydrogen;

R^2 is 3,5-dimethylphenyl-;

R^4 is hydrogen; and

R^5 is 1,1-dimethyl-2-oxo-2-azabicyclo[2.2.1]heptan-7-yl-ethyl-.

In all but one case, M is CH_2CH_2 .

The paucity of examples compared to the enormous scope of the claims, and the lack of any concrete examples of any of the permutations other than those given above for R^1 , R^2 , R^4 and R^5 , raises the question as to whether the underlying technical problem has been shown to be solved over the whole scope of the claimed subject-matter. In the present case, the lack of examples for any but a few of the permutations claimed for R^1 , R^2 , R^4 and R^5 renders the claims unacceptable under Art. 33(3) in conjunction with Art. 5 and 6 PCT because the Applicant has not shown to an acceptable degree that the underlying technical

problem has been solved over the whole scope of the claimed subject-matter.

3.2 Even in the case where the claims could be viewed as being supported over the whole scope of the claimed subject-matter, they would not meet the requirements of Art. 33(3) PCT.

It is clear from D3 that structures containing a pyrrole-like core and having substituents similar or the same as those claimed in the present application have GnRH antagonistic activity. In view of the breadth of the claimed subject-matter in D3, it would appear obvious that other pyrrole-like compounds might have such activity. The breadth of the present claims would also appear to substantiate this argument.

Thus, even if the claims could be seen as being sufficiently supported, they would not meet the requirements of Art. 33(3) PCT in view of their breadth.

The Applicant should also note that these arguments would be further substantiated should the P-documents cited in the International Search Report become relevant to the proceedings.

4. For the assessment of the present claims 1, 17 and 18 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VIII

5. Claims 1, 4, 12, 13 and 15-17 do not meet the requirements of Art. 6 PCT.

The expression "prodrug thereof" does not have a generally-accepted meaning within the art as related to the structures claimed in the present application. Thus, a derivative which constitutes being a pro-drug for one molecule (e.g. an ester) may be completely inactive when applied to another active agent. Since this feature is nothing more than a result to be achieved which has not been defined in

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AUTHORITY (SEPARATE SHEET)**

International application No.
PCT/GB2005/000560

terms of technical features (cf. Rule 6 PCT), it fails to meet the requirements for clarity.